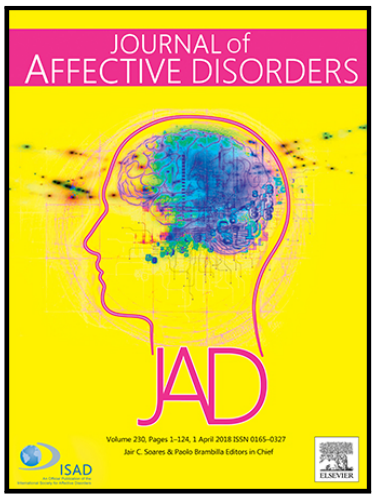

Different Patterns Of Alcohol Consumption And The Incidence And Persistence Of Depressive And Anxiety Symptoms Among Older Adults In Ireland: A Prospective Community-Based Study

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Highlights

- Associations of problematic alcohol use and incident and persistent probable depression and anxiety were assessed in a representative Irish community sample
- Among women, problematic alcohol use was independently associated with incident depressive and anxiety symptoms
- In women, problematic alcohol use was also associated with the persistence of depressive symptoms at a 2-year follow-up

DIFFERENT PATTERNS OF ALCOHOL CONSUMPTION AND THE INCIDENCE AND PERSISTENCE OF DEPRESSIVE AND ANXIETY SYMPTOMS AMONG OLDER ADULTS IN IRELAND: A PROSPECTIVE COMMUNITY-BASED STUDY

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Abstract

Background: The associations of different patterns of alcohol consumption and the incidence and persistence of depressive and anxiety symptoms in older age remain unclear.

Methods: Data on 6095 adults aged ≥ 50 years old from the Irish Longitudinal Study on Aging (TILDA) was analyzed. Participants completed the CAGE instrument to screen for problematic alcohol use at baseline between October 2009 and February 2011. Outcomes were incident (assessed by the CES-D scale) and anxiety (assessed by the Hospital Anxiety and Depressive scale) symptoms after a two-year follow-up as well as persistence of probable depression and anxiety among those with a positive screen for those disorders at baseline. Associations were adjusted for potential confounders through multivariable models.

Results: In the overall sample, problem drinking did not predict incident and persistent depression and anxiety in this sample. Among females, problem drinking increased the risk for incident depression (OR=2.11; 95%CI=1.12-4.00) and anxiety (OR=2.22; 95%CI=1.01-4.86). In addition, problem drinking increased the risk of persistent depressive symptoms (OR=2.43; 95%CI=1.05-5.06) among females.

Conclusion: Problem drinking may increase the risk of incident probable depression and anxiety among older females. Furthermore, problem drinking led to a higher likelihood of persistent depressive symptoms in older female participants. Interventions targeting problem drinking among older females may prevent the onset and persistence of depression in this population, while also decreasing the incidence of anxiety symptoms.

Keywords: Depression; anxiety; alcohol use disorder; older adults; prospective study; psychiatry

1. Introduction

Alcohol use disorder (AUD) frequently co-occurs with depression and anxiety disorders (Chou et al., 2012; Grant et al., 2015; Lai et al., 2015). However, the associations of different patterns of alcohol consumption and incident depression and anxiety among older adults remain unclear. For example, a recent prospective study found that moderate consumption of wine may be associated with a lower risk of incident depression, whilst heavier drinkers appeared to be at higher risk (Gea et al., 2013). Likewise, Almeida et al. (2013) observed that men who were risk-drinkers (defined as those who had consumed more than 4 standard drinks daily) had a higher risk of incident late-life depression whereas non-risk drinking in conjunction with at least another lifestyle habit was protective. Nevertheless, a recent study found that frequent-drinkers were not at increased risk of developing depression in a prospective Chinese sample of older adults (Cheng et al., 2016), whilst a Dutch study found no association of the level of alcohol intake and incident depression in a sample of older adults (Koster et al., 2006). Differences in the assessment and definition of the exposure (i.e. alcohol use) and outcome (i.e., depression) variables as well as variations in sample characteristics across studies may partly explain those discrepant findings.

Late-life generalized anxiety disorder (GAD) or even subthreshold forms of this illness appear to be associated with significant disability (Miloyan et al., 2015). Furthermore, anxiety frequently co-occurs with late-life depression (Ramos and Stanley, 2018). Relatively few studies have examined the associations between different levels of alcohol consumption and incident anxiety in mid and late-life at a population level (Wu and Blazer, 2014). High-risk alcohol drinkers relative to either low- or moderate-risk drinkers had higher prevalence rates of co-morbid depression as well as anxiety disorder among participants aged 60+ years from the US 2000-2001 NESARC study (Sacco et al., 2009). However, DSM-IV alcohol use

disorders were not associated with incident GAD in a 3-year follow-up study that enrolled a representative population based-sample from the US aged 60+ years (Chou et al., 2011).

Prospective studies in adolescents and younger adults have found that alcohol use disorders or heavy-drinking may predict incident depression only among females (Fleming et al., 2008; Wang and Patten, 2001), while other studies found that these associations are present in either sex (Boden and Fergusson, 2011; Lee et al., 2018a). Furthermore, to our knowledge no population-wide study to date have investigated the effects of varying levels of alcohol intake on the persistence of anxiety and depressive symptoms specifically among older adults with a positive screen for those disorders at baseline.

Due to these gaps in the literature, the current prospective study aimed to assess whether different levels of alcohol consumption could be independently associated with varying risks to develop depressive and anxiety symptoms in a representative community-dwelling sample of older adults living in Ireland. In addition, we also aimed to investigate whether those associations could vary as a function of gender. Thus, analysis stratified by gender were also conducted. Finally, we investigated the role of different levels of alcohol intake on the persistence of depressive and anxiety symptoms in this population.

2. Methods

2.1. Study design and sample

We analyzed data from two consecutive waves of the Irish Longitudinal Study on Ageing (TILDA) survey. Data are publically available through the website http://tilda.tcd.ie/. Full details of the survey including its sampling methods have been described in detail elsewhere (Cronin et al., 2013; Kearney et al., 2011; Whelan and Savva, 2013). Briefly, this was a community-based survey of older adults residing in Ireland conducted by Trinity College Dublin. The first wave (W1) or the baseline survey was conducted between October 2009 and February 2011, and the second wave (W2) was undertaken between April 2012 and January 2013. The target sample consisted of all individuals living in private households aged 50 and over in Ireland. Clustered random sampling was used to obtain nationally representative samples. The institutionalized, and those with a doctor's diagnosis of dementia were excluded from W1. In addition, those who were judged to be unable to participate in the survey because of cognitive impairment (judged at the interviewer's discretion) were also excluded from W1. Trained personnel conducted interviews with the use of Computer Assisted Personal Interviewing (CAPI). For sensitive questions, participants were asked to fill in a self-completion questionnaire (SCQ), which was returned after the interview. The response rate of W1 was 62%, and of those who participated in W1, 84% returned the SCQ (Kearney et al., 2011; Whelan and Savva, 2013). Sampling weights were generated with respect to age, sex and educational attainment to the Quarterly National Household Survey 2010. Ethical approval for TILDA was obtained by the Faculty of Health Sciences Ethics Committee of Trinity College Dublin. Written informed consent was obtained from all participants.

2.2. Measures

2.2.1. Alcohol consumption

The CAGE screening test, which has been validated across different cultures and age groups to identify alcohol use disorders (AUDs) was used (Chan et al., 1994; Mayfield et al., 1974; Steinbach, 1992). The CAGE instrument assesses four aspects of drinking with the following questions: (a) Have you ever felt you should cut down on your drinking?; (b) Have people annoyed you by criticizing your drinking?; (c) Have you ever felt bad or guilty about your drinking?; and (d) Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover? These questions had answer options 'yes' (scored=1) or 'no' (scored=0). The scores were summed to create a scale ranging from 0-4. Problem drinking was defined as a score of ≥2 (Mayfield et al., 1974). This cut-off of ≥2 has been shown to have high sensitivity and specificity for the screening of problem drinking in older adults (Buchsbaum et al., 1992). Based on this threshold, participants were categorized into non-drinkers, non-problem drinkers (CAGE score ≤1), and problem drinkers (CAGE score ≥2). Non-drinkers referred to those who claimed to not drink alcohol or reported to not have consumed any alcohol beverages (e.g., beer, cider, wine, spirits, cocktails) in the last 6 months.

In line with a previous publication using the same dataset (Cousins et al., 2014), we also categorized individuals into non-drinkers, light/moderate drinkers, or heavier drinkers. The above-mentioned definition was used for non-drinkers. Self-reported information on quantity and frequency of alcohol use in the last 6 months was used to calculate the number of drinks consumed per day and week (Dawson, 2003). The cut-off used to identify heavier drinkers was based on a modified version of the recommendations of the National Institute on Alcohol Abuse and Alcoholism (NIAAA) (National Institute on Alcohol Abuse and Alcoholism, 2005) to reflect the amount of alcohol contained in a standard drink in the Irish content (Hope, 2009; Rehm and Patra, 2012). Specifically, the threshold used to define heavier drinkers was >4 standard drinks per day or >10 drinks per week (Cousins et al.,

2014). All other individuals who were not heavier drinkers or non-drinkers were classified as light/moderate drinkers.

2.2.2. Anxiety and depressive symptoms

The same method of assessment for both depression and anxiety at W1 and W2 were employed. The scale used for depressive symptoms was the 20-item Center for Epidemiologic Studies Depression (CES-D) (Radloff, 1977), which assesses symptoms experienced in the seven days preceding the survey. The 20 items were scored on scales from 0 (rarely or none of the time, less than one day in the week) to 3 (most or all of the time, five to seven days in the week) with four items reverse coded (recoded so that all items were based on the same scale). Scores were summed to create a scale that ranged from 0 to 60, with higher scores indicating more depressive symptoms. The validity of the CES-D scale as a measure of depression in community-dwelling older adults has been well-documented (Hertzog et al., 1990; Lewinsohn et al., 1997). A positive screen for depression was defined as a cutoff score ≥16. This cut-off point has been associated with 100% sensitivity and 88% specificity for major depression in community-dwelling older adults (Beekman et al., 1997).

Anxiety symptoms were assessed with the anxiety subscale of the Hospital Anxiety and Depression Scale (HADS-A) (Zigmond and Snaith, 1983). This instrument consists of seven items rated on a four-point scale from 0 (not at all) to 3 (very often indeed), with five items reverse coded. The scores of the seven items were summed to create a scale that ranged from 0 to 21, with higher scores indicating more symptoms of anxiety. The HADS-A has been found to have good sensitivity and specificity for assessing anxiety disorders across all ages in the general population (Bjelland et al., 2002), and among specific age groups of older adults (Spinhoven et al., 1997). A positive screen for GAD was defined as a score of ≥8. This cut-off point has been associated with 89% sensitivity and 75% specificity for the screening of GAD (Bjelland et al., 2002; Olssøn et al., 2005).

2.2.3. Control variables

Sociodemographic characteristics included sex, age (50-59, 60-69, 70-79, and ≥80 years), marital status (married/cohabiting, never married, separated/divorced/never married). education (primary, secondary, tertiary), and employment status. Current employment status was categorized as: employed (employed and self-employed, including farming); retired; and unemployed (unemployed, permanently sick or disabled, looking after home or family, or in education or training).

A total of 17 chronic medical conditions were assessed [high blood pressure or hypertension; angina; heart attack (including myocardial or coronary thrombosis); congestive heart failure; diabetes or high blood sugar; stroke (cerebral vascular disease); ministroke or transient ischemic attack; high cholesterol; heart murmur; abnormal heart rhythm; any other heart trouble; chronic lung disease such as chronic bronchitis or emphysema; asthma; arthritis (including osteoarthritis, or rheumatism); osteoporosis; cancer or a malignant tumor (including leukemia or lymphoma but excluding minor skin cancers); cirrhosis or serious liver damage]. The participant was shown a card with the medical conditions and was instructed to indicate the conditions for which the participant has ever received a doctor's diagnosis. The total number of chronic medical conditions was calculated and categorized as 0 (none), 1, or ≥2.

2.3. Statistical analysis

A total of 8504 people aged ≥50 years (n=8175) and their spouses or partners younger than 50 years (n=329) participated in W1. Of these 8504 people, 7,207 were followed at W2. Our analytical sample consisted of: (a) participants aged 50 years and over at W1 who returned the W1 SCQ; and (b) those who provided data on anxiety and/or depression at W2. These restrictions were imposed as information on alcohol consumption and some other variables used in the analysis were obtained from the SCQ at W1. In addition, the only variables from

W2 that were used in the analysis were anxiety and depression. Thus, the final sample consisted of 6,095 individuals.

Analysis was done with Stata version 14.1 (Stata Corp LP, College Station, Texas). The difference in baseline sample characteristics by drinking pattern (i.e., non-drinker, non-problematic, problematic) was tested by χ^2 tests. Multivariable logistic regression analysis was used to assess the associations between drinking patterns at baseline and depression or anxiety. The exposure variables were the two drinking patterns assessed in the current study [i.e., (a) non-drinker/non-problem drinker/problem drinker (i.e. with a positive screen according to the CAGE); (b) non-drinker/light or moderate drinker/heavier drinker]. The four outcomes were incident depression, incident anxiety, persistent depression, and persistent anxiety. Incident depression and anxiety were assessed among those without depression or anxiety respectively at baseline (W1), and referred to new cases of depression or anxiety at W2 (outcome). Thus, those with depression at baseline were omitted from the analysis on incident depression, and similarly, those with anxiety at W1 were excluded from the analysis on incident anxiety. On the other hand, persistent depression and anxiety were evaluated only among those who had depression or anxiety at W1 respectively, and were defined as the presence of depression or anxiety at W2. The models were adjusted for sex, age, marital status, education, employment status, number of chronic conditions based on information obtained at W1. The selection of control variables was based on past literature (Bellos et al., 2016). In addition, we tested for interaction by sex by including the product term 'drinking pattern X sex' in regression analysis of the overall sample. We also conducted analyses stratified by sex as previous research has shown that sex may modify the association between alcohol consumption and mental health outcomes. These analyses were not adjusted for sex.

All variables were included in the models as categorical variables. The sample weighting and the complex study design including clustering within households were taken

into account to obtain nationally representative estimates using the Stata *svy* command. Only the frequencies (n) are presented as unweighted estimates. Results are expressed as odds ratios (ORs) and 95% confidence intervals (95%CIs). A *p*-value <0.05 was considered to be statistically significant.

3. Results

The mean age (standard deviation; SD) of the analytical sample (N=6095) was 63.3 (9.0) years, and 51.7% were females. The prevalence of a positive screen for depression and anxiety at baseline were 9.8% (n=532) [Females 12.3% (n=359) vs. Males 7.1% (n=173)] and 24.9% (n=1418) [Females 28.7% (n=893) vs. Males 20.9% (n=525)] respectively. At two-year follow-up, there were 265 (161 females and 104 males) and 165 (113 females and 52 males) new cases of incident depression and anxiety respectively. Of those who had depression or anxiety at baseline, 41.0% (Females 40.2% vs. Males 42.2%) and 35.2% (Females 39.0% vs. Males 29.9%) continued to have these conditions at two-year follow-up respectively.

The prevalence of drinkers without a positive screen for problem drinking was 59.1% (Females vs. Males: 57.4% vs. 60.4%), while 11.7% (Females vs. Males: 7.8% vs. 15.8%) had a positive screen for problem drinking according to the CAGE instrument. The corresponding figures for light/moderate drinking and heavier drinking were 42.7% (Females vs. Males: 49.0% vs. 36.0%) and 27.3% (Females vs. Males: 25.0% vs. 40.0%) respectively. Baseline characteristics of the overall sample compared to those who screened positive for problem drinking are presented in **Table 1**. Nearly 2/3 of those with a positive screen for problem drinking were males and they tended to be younger and to have a higher education. The prevalence of depressive and anxiety symptoms was highest among those with a positive screen for problem drinking and lowest among non-problem drinkers. Of those who were non-problem drinkers, 70.0% and 30.0% were light/moderate and heavier drinkers, respectively. The corresponding figures among those who were problem drinkers were 27.0% and 73.0%, respectively. Among light/moderate drinkers, 92.9% and 7.1% were non-problem drinkers and problem drinkers, respectively, while for heavy drinkers, the corresponding figures were 67.5% and 32.5%, respectively (Table 1).

<Please insert Table 1 here>

The overall associations of a positive screen for problem drinking and other covariates with incident/persistent depression and anxiety estimated by multivariable logistic regression are presented in **Table 2**. In the overall sample, a positive screen for problem drinking did not predict incident/persistent anxiety or depression when the reference category was non-drinkers. However, when the reference category was non-problem drinkers, problem drinking at baseline was associated with a higher risk for incident anxiety. In the overall sample, interaction analysis showed that this sex difference was significantly only for persistent depression (Figure 1). However, in analysis stratified by sex, a positive screen for problem drinking predicted incident depression and anxiety as well as persistent depression only among females even after multivariable adjustment to potential confounders (**Table 3**). Specifically, among females with no depression at baseline, those with a positive screen for problem drinking at baseline had a significant 2.11 (95%CI=1.12-4.00) times higher odds of developing depressive symptoms at follow-up, compared to non-drinkers. The corresponding figure for incident anxiety symptoms (among females without a positive screen for anxiety at baseline) was OR 2.22 (95%CI=1.01-4.86). Among women who had depression at baseline, a positive screen for problem drinking at Wave 1 predicted the persistence of depressive symptoms at follow-up (OR 2.43; 95%CI=1.05-5.60). Furthermore, females who screened positive for problem drinking also exhibited a higher risk of incident depressive and anxiety symptoms as well as persistent depression at follow-up when compared to non-problem drinkers. Finally, when alcohol consumption was categorized as non-drinkers, light/moderate drinkers, heavier drinkers, no meaningful differences in assessed mental health outcomes at follow-up emerged (**Table 4**).

<Please insert Figure 1 here>

<Please insert Table 2 here>

<Please insert Table 3 here>

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4. Discussion

The current study found that in nationally representative sample of mid to late-life adults a positive screening for problem drinking according to the CAGE questionnaire was associated with a greater likelihood of developing depressive as well as anxiety symptoms only among females. Furthermore, among women a positive screen for problem drinking was associated with the persistence of depressive symptoms. Nevertheless, when only the quantity of alcohol consumption was considered for categorization of alcohol consumption (i.e., non-drinkers; light/moderate drinkers and heavier drinkers) no associations with either the development or persistent of depressive and anxiety symptoms was evident. A recent systematic review conducted by Wu and Blazer (2014) pointed to the paucity of prospective studies that assessed the possible association of different patterns of alcohol consumption and incident mood and anxiety disorders.

Some studies have suggested that either light or non-risk drinking may protect against the emergence of depression in late-life (Almeida et al., 2013; Gea et al., 2013). However, the categorization of alcohol consumption based solely on the quantity of alcohol intake may be fraught with biases (Naimi et al., 2017). For example, it has been noted that observational studies tend to overestimate the frequency of ‘moderate’ drinkers relative to non-drinkers, and that methodological attempts to control for such a selection bias tend to attenuate associations between ‘moderate’ drinking and beneficial health outcomes including possible preventative effects upon mortality (Naimi et al., 2017). Our findings suggest that problem drinking may confer a higher risk of incident depressive and anxiety symptoms exclusively on females. However, it is worthy to note that the NESARC study found no evidence for an association of alcohol use disorders (AUDs) and incident DSM-IV major depressive disorder

(MDD) or GAD in a nationally representative US sample was observed (Chou et al., 2011). It should be noted, however, that the NESARC study used structured diagnostic interviews to establish DSM-IV diagnoses, whilst our study used validated screening tools. The CAGE has robust receiver operating characteristic (ROC) properties for the screening of DSM-IV alcohol dependence among older adults (Caputo et al., 2012). However, the psychometric properties of the CAGE for screening of AUDs based on less stringent (i.e. more inclusive) DSM-5 criteria remains unknown (Hasin et al., 2013). In addition, the CAGE does not screen for the presence of lifetime AUDs. Moreover, the study conducted by Chou et al. (2011) adjusted estimates for a wide array of DSM-IV mental disorders including personality disorders, and hence this may also contribute to discrepant results between their study and ours.

A novel finding of our work is that the associations of a positive screen for problem drinking and incident depressive and anxiety symptoms were observed only among females. To our knowledge no previous prospective, population-wide, study has found this pattern of association specifically among mid and late-life adults. However, previous studies conducted in samples of adolescents or younger adults have found that the association of AUDs (or heavier alcohol consumption) and depression was restricted to females (Fleming et al., 2008; Wang and Patten, 2001), whilst other studies found that the association was relevant irrespective of sex (Boden and Fergusson, 2011; Lee et al., 2018a). Several mechanisms may explain this finding. For example, preclinical studies found that female mice are more vulnerable to the neuroinflammatory effects of ethanol (Pascual et al., 2017), and aberrant inflammation may contribute to the emergence of depression (Köhler et al., 2017; Maes et al., 2011; Miller and Raison, 2016). Moreover, in an aging cohort a significant difference in cortisol awakening responses were reported for women who were heavier drinkers as compared to moderate drinkers, whereas a similar effect was not observed for men (Badrick

et al., 2008). This finding suggest that risk drinking can be more detrimental to the hypothalamic-pituitary-adrenal (HPA) axis in older women as compared to older men. This mechanism may also contribute to the specific association between problem drinking and depression and anxiety observed for older women in our study. In addition, women have a lower percentage of body water compared to men of similar body mass, and hence achieve higher blood alcohol concentrations after consuming similar amounts of alcohol (Erol and Karpyak, 2015). In addition, the smaller volume of distribution in women compared to men is also associated with a longer persistence of elevated blood ethanol levels (Erol and Karpyak, 2015). Those sex differences in alcohol pharmacokinetics may also partly explain our findings. Consistently we also observed that a positive screen for problem drinking was associated with the persistence of depressive symptoms only among females. Furthermore, a previous Mendelian randomization study found no evidence for a causal association between the consumption of more than six daily drinks an incident depression in a sample of older Australian men (Almeida et al., 2014), and hence this study further suggests that among older men the association of heavier drinking and incident depression is unlikely to be causal.

4.1. Strengths and limitations

The findings of the current study should be interpreted within its limitations. First, a positive screen for depression and anxiety does not substantiate these diagnoses. However, evidence suggest that GAD during late-life should be more accurately conceived on a dimensional basis (Miloyan et al., 2015). In addition, depression appears to occur on a continuum of severity ranging from subthreshold depression to full-blown MDD, with the former being a risk factor for the later (Lee et al., 2018b). In addition, we used an a priori defined cutoff score for the CES-D thus avoiding potential biases (Levis et al., 2017). Second, although our findings were adjusted for a range of sociodemographic and clinical variables residual confounding is still possible. For example, it is possible that participants with a history of

previous depressive episodes could be more likely to have a co-occurring AUD (Boden and Fergusson, 2011). Third, the short follow-up time (2 years) may not be sufficient to allow an impact of different patterns of alcohol consumption on mental health outcomes. Fourth, the data is based on self-report, and hence reporting bias may exist. Finally, those who were not followed at W2 were more likely to have been older, unemployed, not married/cohabiting, and of lower education at baseline. Thus, some degree of bias might have been introduced due to selective loss to follow-up.

The strengths of this study include the use of a nationally-representative sample of the Irish population, its prospective design and the use of validated instruments. To our knowledge this is one of the few population-wide prospective studies that investigated an association with different patterns of alcohol intake and incident depressive and anxiety symptoms in older age. In addition, we could demonstrate that detrimental effects of a positive screen for problem drinking on incident depressive and anxiety symptoms appears to be restricted to the female gender among older adults.

4.2. Clinical and public health implications

The present observational study suggests that problem drinking may be associated with a higher incidence of depression and anxiety only among older women. If replicated this finding may have clinical and research relevance. The most obvious implication is that older females with problem drinking may be an at-risk population for the emergence of depression and anxiety symptoms. Therefore, efforts directed to the early recognition and management of problem drinking in this population may ultimately decrease the burden of late-life depression and anxiety. It has also been suggested that people may consume alcohol as an attempt to self-medicate depressive symptoms. Our findings suggest that among older females this may contribute to the persistence of depressive symptoms. Therefore, clinicians

treating older patients with co-morbid AUD and depression should be aware of the potential detrimental consequences of problem drinking especially among females.

4.3. Conclusion

Our findings demonstrate that a positive screen for problem drinking increases the risk of incident depressive and anxiety symptoms only among females. Furthermore, a positive screening for problem drinking increased the likelihood of persistent depression only in females. The design of Mendelian randomization studies providing a more stringent control of confounders could be a next step to investigate the causality of these associations, while randomized controlled trials targeting AUD among older females may lead to the prevention of depressive and anxiety symptoms in this population.

Author statement

AFC and AK conceived and designed the study. AFC and AK wrote the first draft of the manuscript. AFC, BS, MM, MS, DV, PAK, ARB, MIH, and AK interpreted the data. BS, MM, MS, DV, PAK, ARB, and MIH provided significant intellectual contribution to the manuscript. All authors have read and approved the final version of the manuscript prior to submission.

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project has been designed and implemented by the TILDA Study Team © Department of Health and Children. Copyright and all other intellectual property rights relating to the data are vested in TILDA .AK's work was supported by the Miguel Servet contract financed by the CP13/00150 and PI15/00862 projects, integrated into the National R + D + I and funded by the ISCIII - General Branch Evaluation and Promotion of Health Research - and the European Regional Development Fund (ERDF-FEDER).

Conflct of interest

None.

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FIGURE LEGEND

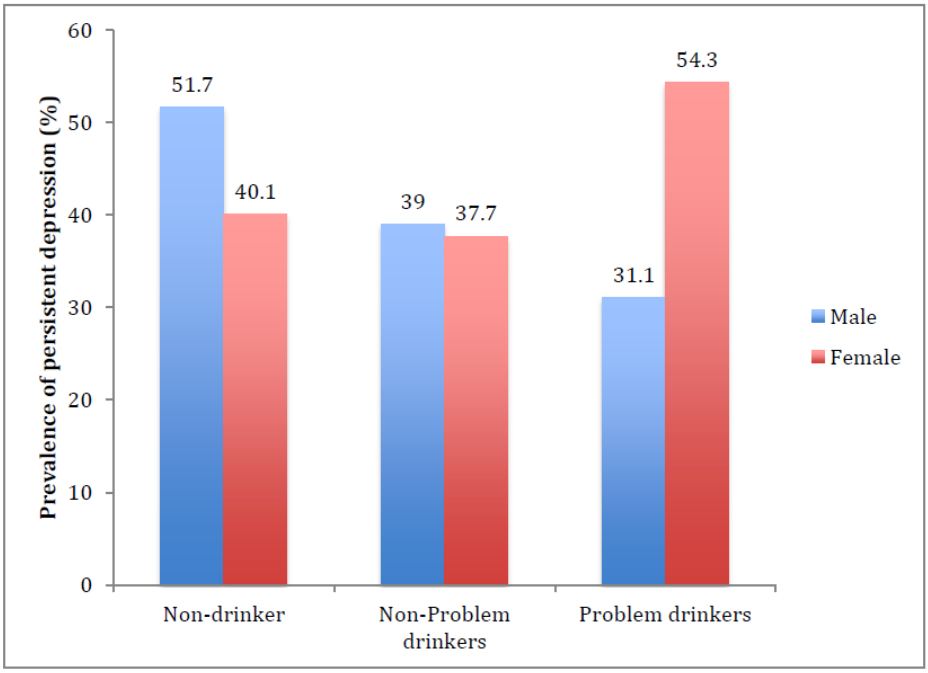

Fig. 1. Prevalence of persistent depression by problematic drinking status by sex
Abbreviation: AUD Alcohol use disorder.
Analysis was restricted to those who had a positive screen for depression at Wave 1.
Persistent depression was defined as having a positive screen for depression at Wave 1 and Wave 2.

References

Almeida, O.P., Hankey, G.J., Yeap, B.B., Golledge, J., Flicker, L., 2014. The triangular association of ADH1B genetic polymorphism, alcohol consumption and the risk of depression in older men. Molecular psychiatry 19, 995-1000.
Almeida, O.P., Hankey, G.J., Yeap, B.B., Golledge, J., McCaul, K., Flicker, L., 2013. A risk table to assist health practitioners assess and prevent the onset of depression in later life. Preventive medicine 57, 878-882.
Badrick, E., Bobak, M., Britton, A., Kirschbaum, C., Marmot, M., Kumari, M., 2008. The relationship between alcohol consumption and cortisol secretion in an aging cohort. The Journal of clinical endocrinology and metabolism 93, 750-757.
Beekman, A.T., Deeg, D.J., Van Limbeek, J., Braam, A.W., De Vries, M.Z., Van Tilburg, W., 1997. Criterion validity of the Center for Epidemiologic Studies Depression scale (CES-D): results from a community-based sample of older subjects in The Netherlands. Psychological medicine 27, 231-235.
Bellos, S., Skapinakis, P., Rai, D., Zitko, P., Araya, R., Lewis, G., Lionis, C., Mavreas, V., 2016. Longitudinal association between different levels of alcohol consumption and a new onset of depression and generalized anxiety disorder: Results from an international study in primary care. Psychiatry research 243, 30-34.
Bjelland, I., Dahl, A.A., Haug, T.T., Neckelmann, D., 2002. The validity of the Hospital Anxiety and Depression Scale: an updated literature review. Journal of psychosomatic research 52, 69-77.
Boden, J.M., Fergusson, D.M., 2011. Alcohol and depression. Addiction (Abingdon, England) 106, 906-914.
Buchsbaum, D.G., Buchanan, R.G., Welsh, J., Centor, R.M., Schnoll, S.H., 1992. Screening for drinking disorders in the elderly using the CAGE questionnaire. Journal of the American Geriatrics Society 40, 662-665.
Caputo, F., Vignoli, T., Leggio, L., Addolorato, G., Zoli, G., Bernardi, M., 2012. Alcohol use disorders in the elderly: a brief overview from epidemiology to treatment options. Experimental gerontology 47, 411-416.
Chan, A.W., Pristach, E.A., Welte, J.W., 1994. Detection by the CAGE of alcoholism or heavy drinking in primary care outpatients and the general population. *Journal of Substance Abuse* 6, 123-135.
Cheng, H.G., Chen, S., McBride, O., Phillips, M.R., 2016. Prospective relationship of depressive symptoms, drinking, and tobacco smoking among middle-aged and elderly community-dwelling adults: Results from the China Health and Retirement Longitudinal Study (CHARLS). Journal of affective disorders 195, 136-143.
Chou, K.L., Mackenzie, C.S., Liang, K., Sareen, J., 2011. Three-year incidence and predictors of first-onset of DSM-IV mood, anxiety, and substance use disorders in older adults: results from Wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions. The Journal of clinical psychiatry 72, 144-155.
Chou, S.P., Lee, H.K., Cho, M.J., Park, J.I., Dawson, D.A., Grant, B.F., 2012. Alcohol use disorders, nicotine dependence, and co-occurring mood and anxiety disorders in the United States and South Korea-a cross-national comparison. Alcoholism, clinical and experimental research 36, 654-662.
Cousins, G., Galvin, R., Flood, M., Kennedy, M.C., Motterlini, N., Henman, M.C., Kenny, R.A., Fahey, T., 2014. Potential for alcohol and drug interactions in older adults: evidence from the Irish longitudinal study on ageing. BMC geriatrics 14, 57.

Cronin, H., O'Regan, C., Finucane, C., Kearney, P., Kenny, R.A., 2013. Health and aging: development of the Irish Longitudinal Study on Ageing health assessment. Journal of the American Geriatrics Society 61 Suppl 2, S269-278.
Dawson, D.A., 2003. Methodological issues in measuring alcohol use. Alcohol research & health : the journal of the National Institute on Alcohol Abuse and Alcoholism 27, 18-29.
Erol, A., Karpyak, V.M., 2015. Sex and gender-related differences in alcohol use and its consequences: Contemporary knowledge and future research considerations. Drug and alcohol dependence 156, 1-13.
Fleming, C.B., Mason, W.A., Mazza, J.J., Abbott, R.D., Catalano, R.F., 2008. Latent growth modeling of the relationship between depressive symptoms and substance use during adolescence. Psychology of addictive behaviors : journal of the Society of Psychologists in Addictive Behaviors 22, 186-197.
Gea, A., Beunza, J.J., Estruch, R., Sanchez-Villegas, A., Salas-Salvado, J., Buil-Cosiales, P., Gomez-Gracia, E., Covas, M.I., Corella, D., Fiol, M., Aros, F., Lapetra, J., Lamuela-Raventos, R.M., Warnberg, J., Pinto, X., Serra-Majem, L., Martinez-Gonzalez, M.A., 2013. Alcohol intake, wine consumption and the development of depression: the PREDIMED study. BMC medicine 11, 192.
Grant, B.F., Goldstein, R.B., Saha, T.D., Chou, S.P., Jung, J., Zhang, H., Pickering, R.P., Ruan, W.J., Smith, S.M., Huang, B., Hasin, D.S., 2015. Epidemiology of DSM-5 Alcohol Use Disorder: Results From the National Epidemiologic Survey on Alcohol and Related Conditions III. JAMA psychiatry 72, 757-766.
Hasin, D.S., O'Brien, C.P., Auriacombe, M., Borges, G., Bucholz, K., Budney, A., Compton, W.M., Crowley, T., Ling, W., Petry, N.M., Schuckit, M., Grant, B.F., 2013. DSM-5 criteria for substance use disorders: recommendations and rationale. The American journal of psychiatry 170, 834-851.
Hertzog, C., Van Alstine, J., Usala, P.D., Hultsch, D.F., Dixon, R., 1990. Measurement properties of the Center for Epidemiological Studies Depression Scale (CES-D) in older populations. Psychological Assessment: A Journal of Consulting and Clinical Psychology 2, 64.
Hope, A., 2009. A standard drink in Ireland: what strength? Dublin: Health Service Executive.
Kearney, P.M., Cronin, H., O'Regan, C., Kamiya, Y., Savva, G.M., Whelan, B., Kenny, R., 2011. Cohort profile: the Irish Longitudinal Study on Ageing. International journal of epidemiology 40, 877-884.
Köhler, C., Freitas, T., Maes, M., Andrade, N., Liu, C., Fernandes, B., Stubbs, B., Solmi, M., Veronese, N., Herrmann, N., 2017. Peripheral cytokine and chemokine alterations in depression: a meta - analysis of 82 studies. Acta Psychiatrica Scandinavica 135, 373-387.
Koster, A., Bosma, H., Kempen, G.I., Penninx, B.W., Beekman, A.T., Deeg, D.J., van Eijk, J.T., 2006. Socioeconomic differences in incident depression in older adults: the role of psychosocial factors, physical health status, and behavioral factors. Journal of psychosomatic research 61, 619-627.
Lai, H.M., Cleary, M., Sitharthan, T., Hunt, G.E., 2015. Prevalence of comorbid substance use, anxiety and mood disorders in epidemiological surveys, 1990-2014: A systematic review and meta-analysis. Drug and alcohol dependence 154, 1-13.
Lee, S.B., Chung, S., Lee, H., Seo, J.S., 2018a. The Mutual Relationship Between Men's Drinking and Depression: A 4-Year Longitudinal Analysis. Alcohol and alcoholism (Oxford, Oxfordshire).
Lee, Y., Stockings, E., Harris, M., Doi, S., Page, I., Davidson, S., Barendregt, J., 2018b. The risk of developing major depression among individuals with subthreshold depression: a

systematic review and meta-analysis of longitudinal cohort studies. Psychological medicine, 1-11.
Levis, B., Benedetti, A., Levis, A.W., Ioannidis, J.P.A., Shrier, I., Cuijpers, P., Gilbody, S., Kloda, L.A., McMillan, D., Patten, S.B., Steele, R.J., Ziegelstein, R.C., Bombardier, C.H., de Lima Osorio, F., Fann, J.R., Gjerdingen, D., Lamers, F., Lotrakul, M., Loureiro, S.R., Lowe, B., Shaaban, J., Stafford, L., van Weert, H., Whooley, M.A., Williams, L.S., Wittkampf, K.A., Yeung, A.S., Thombs, B.D., 2017. Selective Cutoff Reporting in Studies of Diagnostic Test Accuracy: A Comparison of Conventional and Individual-Patient-Data Meta-Analyses of the Patient Health Questionnaire-9 Depression Screening Tool. American journal of epidemiology 185, 954-964.
Lewinsohn, P.M., Seeley, J.R., Roberts, R.E., Allen, N.B., 1997. Center for Epidemiologic Studies Depression Scale (CES-D) as a screening instrument for depression among community-residing older adults. Psychology and aging 12, 277-287.
Maes, M., Leonard, B., Fernandez, A., Kubera, M., Nowak, G., Veerhuis, R., Gardner, A., Ruckoanich, P., Geffard, M., Altamura, C., Galecki, P., Berk, M., 2011. (Neuro)inflammation and neuroprogression as new pathways and drug targets in depression: from antioxidants to kinase inhibitors. Progress in neuro-psychopharmacology & biological psychiatry 35, 659-663.
Mayfield, D., McLeod, G., Hall, P., 1974. The CAGE Questionnaire: Validation of a new alcoholism screening instrument. *American Journal of Psychiatry* 131, 1121-1123.
Miller, A.H., Raison, C.L., 2016. The role of inflammation in depression: from evolutionary imperative to modern treatment target. Nature reviews. Immunology 16, 22-34.
Miloyan, B., Byrne, G.J., Pachana, N.A., 2015. Threshold and subthreshold generalized anxiety disorder in later life. The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry 23, 633-641.
Naimi, T.S., Stockwell, T., Zhao, J., Xuan, Z., Dangardt, F., Saitz, R., Liang, W., Chikritzhs, T., 2017. Selection biases in observational studies affect associations between 'moderate'alcohol consumption and mortality. Addiction (Abingdon, England) 112, 207-214.
National Institute on Alcohol Abuse and Alcoholism, 2005. Helping patients who drink too much: a Clinician's guide (2005 edition). US: Department of Health and Human Services.
Olssøn, I., Mykletun, A., Dahl, A.A., 2005. The Hospital Anxiety and Depression Rating Scale: a cross-sectional study of psychometrics and case finding abilities in general practice. BMC psychiatry 5, 46.
Pascual, M., Montesinos, J., Marcos, M., Torres, J.L., Costa-Alba, P., Garcia-Garcia, F., Laso, F.J., Guerri, C., 2017. Gender differences in the inflammatory cytokine and chemokine profiles induced by binge ethanol drinking in adolescence. Addiction biology 22, 1829-1841.
Radloff, L.S., 1977. The CES-D Scale:A Self-Report Depression Scale for Research in the General Population. Applied Psychological Measurement 1, 385-401.
Ramos, K., Stanley, M.A., 2018. Anxiety Disorders in Late Life. The Psychiatric clinics of North America 41, 55-64.
Rehm, J., Patra, J., 2012. Different guidelines for different countries? On the scientific basis of low-risk drinking guidelines and their implications. Drug and alcohol review 31, 156-161.
Sacco, P., Bucholz, K.K., Spitznagel, E.L., 2009. Alcohol use among older adults in the National Epidemiologic Survey on Alcohol and Related Conditions: a latent class analysis. Journal of studies on alcohol and drugs 70, 829-838.
Spinhoven, P., Ormel, J., Sloekers, P.P., Kempen, G.I., Speckens, A.E., Van Hemert, A.M., 1997. A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. Psychological medicine 27, 363-370.
Steinbach, U., 1992. Social networks, institutionalization, and mortality among elderly people in the United States. Journal of gerontology 47, S183-190.

Wang, J., Patten, S.B., 2001. Alcohol consumption and major depression: findings from a follow-up study. Canadian journal of psychiatry. Revue canadienne de psychiatrie 46, 632-638.
Whelan, B.J., Savva, G.M., 2013. Design and methodology of the Irish Longitudinal Study on Ageing. Journal of the American Geriatrics Society 61 Suppl 2, S265-268.
Wu, L.T., Blazer, D.G., 2014. Substance use disorders and psychiatric comorbidity in mid and later life: a review. International journal of epidemiology 43, 304-317.
Zigmond, A.S., Snaith, R.P., 1983. The hospital anxiety and depression scale. Acta psychiatrica scandinavica 67, 361-370.

Table 1 Baseline characteristics of the study sample

			Problem drinking				Alcohol consumption level			
			Non-drinker	CAGE (-)	CAGE (+)		Non-drinker	Light/moderate	Heavier	
			n=1626	n=3648	n=706		n=1579	n=2581	n=1529	
Characteristic	Category	Total	(29.3%)	(59.1%)	(11.7%)	P-value[b]	(30.0%)	(42.7%)	(27.3%)	P-value[b]
Sex	Female	51.7	61.4	50.3	34.5	<0.001	62.1	59.3	28.4	<0.001
	Male	48.3	38.6	49.7	65.5		37.9	40.7	71.6	
Age (years)	50-59	41.4	26.2	45.6	61.0	<0.001	26.1	43.2	58.5	<0.001
	60-69	31.5	30.1	32.8	28.9		29.8	34.9	28.5	
	70-79	19.4	30.0	16.1	8.6		30.4	16.2	10.3	
	≥80	7.7	13.7	5.5	1.4		13.8	5.7	2.7	
Marital status	Married/cohabiting	68.7	61.6	72.5	70.8	<0.001	61.5	72.5	73.3	<0.001
	Never married	9.6	11.0	8.5	11.5		11.2	8.2	9.5	
	Separated/divorced/widowed	21.7	27.4	19.0	17.6		27.4	19.3	17.1	
Education	Primary	36.0	50.6	30.2	24.8	<0.001	50.4	28.7	26.0	<0.001
	Secondary	44.5	37.7	47.3	49.1		37.7	46.5	51.0	
	Tertiary	19.6	11.7	22.5	26.1		11.9	24.8	23.0	
Employment	Employed	37.3	24.1	42.0	47.8	<0.001	24.1	41.5	47.4	<0.001
status	Retired	34.9	41.5	32.9	27.5		41.6	32.8	29.4	
	Unemployed	27.9	34.4	25.2	24.6		34.3	25.7	23.2	
Number of	0	23.7	21.1	24.6	25.4	<0.001	21.2	23.4	27.1	<0.001
chronic conditions	1	27.9	25.0	28.6	31.6		24.9	29.1	30.4	
	≥2	48.4	53.9	46.8	43.0		53.9	47.5	42.5	
Depression	No	90.2	88.2	92.5	84.8	<0.001	88.4	91.2	91.6	0.010
	Yes	9.8	11.8	7.5	15.2		11.6	8.8	8.4	
Anxiety	No	75.1	75.1	77.1	64.6	<0.001	75.0	76.2	74.0	0.341
	Yes	24.9	24.9	22.9	35.4		25.0	23.8	26.0	

Data are weighted percentage.
The Ns are unweighted.
[a] A positive screen for alcohol use disorder (AUD) was based on a CAGE score ≥2.
[b] Difference in baseline characteristics by drinking pattern was tested by χ^2 tests.

Table 2 The association of a positive screen for problem drinking, sociodemographic factors, and chronic medical conditions with incident or persistent depression and anxiety (overall)

		Incident				Persistent			
		Depression (N=5481)		Anxiety (N=4461)		Depression (N=532)		Anxiety (N=1418)	
Characteristic	Category	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Drinking pattern[a]	Non-drinker	1.00		1.00		1.00		1.00	
	'Other' drinker	1.07	[0.76,1.50]	0.73	[0.48,1.11]	0.91	[0.60,1.40]	0.99	[0.72,1.35]
	Positive screen for problem drinking[a]	1.59	[0.96,2.63]	1.71[b]	[0.90,3.27]	1.17	[0.65,2.11]	1.18	[0.78,1.77]
Sex	Female	1.00		1.00		1.00		1.00	
	Male	0.75	[0.56,1.02]	0.52**	[0.34,0.80]	1.30	[0.83,2.04]	0.67**	[0.51,0.87]
Age (years)	50-59	1.00		1.00		1.00		1.00	
	60-69	0.51***	[0.35,0.74]	0.37***	[0.22,0.62]	0.59	[0.35,1.00]	0.71*	[0.53,0.95]
	70-79	0.37***	[0.24,0.60]	0.51*	[0.28,0.92]	1.09	[0.57,2.10]	0.55**	[0.35,0.85]
	≥80	0.42*	[0.21,0.85]	0.30*	[0.12,0.79]	0.63	[0.18,2.20]	0.57	[0.26,1.24]
Marital status	Married/cohabiting	1.00		1.00		1.00		1.00	
	Never married	0.92	[0.58,1.48]	0.92	[0.47,1.82]	0.65	[0.33,1.29]	0.89	[0.57,1.39]
	Separated/divorced/widowed	1.20	[0.82,1.77]	1.16	[0.71,1.91]	1.14	[0.72,1.80]	0.78	[0.56,1.09]
Education	Primary	1.00		1.00		1.00		1.00	
	Secondary	0.70*	[0.50,0.99]	0.75	[0.48,1.18]	0.75	[0.47,1.20]	0.73*	[0.54,0.99]
	Tertiary	0.67*	[0.46,0.97]	0.65	[0.39,1.09]	0.90	[0.52,1.56]	0.86	[0.61,1.21]
Employment status	Employed	1.00		1.00		1.00		1.00	
	Retired	1.42	[0.98,2.05]	1.48	[0.85,2.57]	1.59	[0.85,2.95]	1.12	[0.77,1.63]
	Unemployed	1.28	[0.88,1.87]	1.87*	[1.15,3.04]	2.13**	[1.31,3.45]	1.30	[0.94,1.81]
Number of chronic conditions	0	1.00		1.00		1.00		1.00	
	1	1.40	[0.90,2.17]	1.09	[0.67,1.76]	1.49	[0.76,2.89]	1.76**	[1.22,2.53]
	≥2	2.26***	[1.56,3.29]	1.54	[0.98,2.43]	1.73	[0.94,3.17]	2.03***	[1.46,2.83]

Abbreviation: OR Odds ratio; CI Confidence interval.
Models are adjusted for all covariates in the table.
[a] CAGE score ≥2.
[b] Significantly different from non-problem drinker ($p<0.05$).
* $p<0.05$, ** $p<0.01$, *** $p<0.001$

Table 3 The association of problem drinking[a] with incident or persistent depression and anxiety by sex

	Incident				Persistent			
	Depression		Anxiety		Depression		Anxiety	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Males								
Non-drinker	1.00		1.00		1.00		1.00	
Non-problem drinker	0.93	[0.54,1.62]	0.53	[0.25,1.13]	0.86	[0.37,1.99]	0.90	[0.52,1.57]
Problem drinker[a]	1.21	[0.61,2.41]	1.23	[0.45,3.35]	0.61	[0.23,1.58]	0.95	[0.51,1.78]
Females								
Non-drinker	1.00		1.00		1.00		1.00	
Non-problem drinker	1.18	[0.78,1.79]	0.82	[0.51,1.33]	1.03	[0.59,1.80]	1.05	[0.73,1.52]
Problem drinker	2.11*[, b]	[1.12,4.00]	2.22*[, b]	[1.01,4.86]	2.43*[, b]	[1.05,5.60]	1.40	[0.82,2.41]

Abbreviation: OR Odds ratio; CI Confidence interval.
Models are adjusted for age, marital status, education, employment status, and number of chronic conditions.
The sample sizes were: incident depression (female N=2909; male N=2572); incident anxiety (female N=2290; male N=2171); persistent depression (female N=359; male N=173); persistent anxiety (female N=893; male N=525).
[a] Problematic drinking was assessed with the CAGE questionnaire. Problematic drinking referred to CAGE score ≥2.
[b] Significantly different from non-problematic drinker (p<0.05).
* p<0.05

Table 4 The association of light/moderate/heavier drinking with incident or persistent depression and anxiety (overall and by sex)

	Incident				Persistent			
	Depression		Anxiety		Depression		Anxiety	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Both sexes[a]								
Non-drinker	1.00		1.00		1.00		1.00	
Light/moderate drinker	1.16	[0.82,1.65]	0.82	[0.54,1.24]	0.99	[0.62,1.57]	1.13	[0.82,1.55]
Heavier drinker	1.01	[0.65,1.56]	0.95	[0.54,1.66]	0.85	[0.47,1.51]	1.00	[0.69,1.45]
Males[b]								
Non-drinker	1.00		1.00		1.00		1.00	

Light/moderate drinker	1.14	[0.63,2.05]	0.61	[0.28,1.37]	0.79	[0.31,2.01]	1.09	[0.59,2.02]
Heavier drinker	1.04	[0.58,1.87]	0.71	[0.30,1.68]	0.70	[0.28,1.72]	1.04	[0.57,1.88]
Females[b]								
Non-drinker	1.00		1.00		1.00		1.00	
Light/moderate drinker	1.20	[0.79,1.83]	0.90	[0.55,1.47]	1.20	[0.67,2.13]	1.18	[0.81,1.72]
Heavier drinker	0.94	[0.50,1.79]	1.18	[0.59,2.34]	1.07	[0.49,2.38]	0.94	[0.58,1.50]

Abbreviation: OR Odds ratio; CI Confidence interval.
[a] Models are adjusted for sex, age, marital status, education, employment status, and number of chronic conditions.
[b] Models are adjusted for age, marital status, education, employment status, and number of chronic conditions.
The sample sizes were: incident depression (total N=5481; female N=2909; male N=2572); incident anxiety (total N=4461; female N=2290; male N=2171); persistent depression (total N=532; female N=359; male N=173); persistent anxiety (total N=1418; female N=893; male N=525).